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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/029,407	12/26/2001	Larry Caldwell	TOPI-002CIP	3764

24353 7590 12/18/2007

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EXAMINER
GHALI, ISIS A D

ART UNIT	PAPER NUMBER
1615	

MAIL DATE	DELIVERY MODE
12/18/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/029,407	CALDWELL ET AL.	
	Examiner	Art Unit	
	Isis A. Ghali	1615	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *05 October 2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-28* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-28* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

The receipt is acknowledged applicants' amendment filed 10/05/2007.

Claims 1-28 are pending and included in the prosecution.

The following rejection has been overcome by virtue of applicants' amendment and remarks:

The rejection of claims 1-28 under 35 U.S.C. 112, second paragraph as being indefinite.

The following rejection has been discussed in the previous office action and is maintained for reasons of record:

Claim Rejections - 35 USC § 103

1. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

2. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of

the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

3. Claims 1-28 are rejected under 35 U.S.C. 103(a) as being unpatentable over US 6,139,861 ('861) combined with US 5,725,874 ('874).

US '861 teaches treatment of migraine or tension headache by topical administration to the mucous membrane of the mouth a NSAID including ibuprofen and ketoprofen (abstract; col.3, lines 40-43). Examples 1 and 3 show that NSAID is the only active agent present in the topical formulation.

Although US '861 realized that migraine and tension headache can be treated by topical administration of NSAID as the only active agent present in the formulation, however, US '861 does not specifically teach administration to the skin.

US '874 teaches percutaneously absorbable formulation that is extremely safe and causes little side effects wherein the formulation can be in the form of cream of patch to deliver NSAID such as of indomethacin, ketoprofen, diclofenac, and ibuprofen (abstract; col.2, lines 61-62; col.3, lines 35-37).

Therefore, it would have been obvious to one having ordinary skill in the art at the time of the invention to treat migraine or tension headache by topical administration

of NSAID as disclosed by US '861, and administer the NSAID topically to the skin in form of cream or patch as disclosed by US '874, motivated by the teaching of US '874 that topical administration of NSAID to the skin is extremely safe and causes little side effects, with reasonable expectation of successfully treating migraine or tension headache by administering to the skin a topical formulation comprising NSAID as the only active agent.

Regarding the kit including written instruction to the consumer, as recited by claims 19-23, the written instruction does not make the claims patentable. See *In re Ngai* 03-1524.

Response to Arguments

4. Applicant's arguments filed 10/05/2007 have been fully considered but they are not persuasive.

Applicants traverse this rejection by arguing that the present invention requires topical application to specific sites of the skin without any systemic effects. Applicants provide documents to show that there is difference between topical and transdermal delivery.

In response to this argument, and with careful review to the provided documents, it is argued that it is the formulation including the drug that controls the delivery of the drug, and since applicants not disclosing any formulation, then the cited prior art reads on the claims. Applicants' disclosure does not exclude systemic delivery. In page 7, lines 19-20, applicants stated that: "A feature of the subject methods is that they result

in no or substantially no side toxic side effects which are observed in systemic delivery, e.g., oral, NSAID delivery mechanisms". The present invention therefore reduces side effects obtained from oral administration by topical application. When drug is applied to the skin, its diffusion is controlled by the nature of the drug if it is lipophilic or hydrophilic, as well as with the composition of the topical formulation. The article "Topical analgesics" provided by applicants, table in page 62, shows that the topical and transdermal formulations are different, and the transdermal formulation requires permeation enhancers. Further the same table shows that topical formulation shows serum level, however insignificant, and can show side effects, however unlikely. In absence of disclosure of any topical composition, the cited prior art reads on the claims because it teaches topical relieve of the underlying condition. Applicants disclosed topical formulations including gels, creams, etc., without disclosing any composition that makes NSAID acts only locally without any systemic effects.

Applicants argue that Friedman teaches applying NSAID to localized area of the mucosa that has a mechanism of action different from the present invention, and does not disclose application of the NSAID to the skin. Applicants argue that application to the mucous membrane permits rapid delivery to the system circulation.

In response to this argument, it is argued that Friedman is relied upon for teaching topical application of NSAID as the only drug in the topical formulation. The formulation disclosed by Friedman is topical formulation, claim 1, and is selected from the same formulations disclosed by applicants including gel, cream, patches, etc.

Friedman disclosed that topical formulation applied to the mucous membrane is absorbed rapidly, and acts locally on the underlying tissue, plexus formed from the branches of the maxillary nerve. Friedman is therefore is relied upon for teaching the ability of NSAID to be delivered from topical formulation to the under lying tissues as the sole active ingredient in the formulation. However, Friedman does not teach topical skin delivery of formulation comprising NSAID as the only active agent, and therefore Oda is relied upon for teaching that NSAID can be delivered topically to the skin. Additionally, in response to applicant's arguments against the references individually, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.*, 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986).

Applicants argue that Oda teaches only systemic delivery of the NSAID and drugs only effective when enter the blood. The combined teaching of Friedman and Oda does not teach the present invention.

In response to this argument, it is argued that Oda teaches the same formulations disclosed by applicants including gel, cream, patches, etc. Oda is relied upon for the teaching of the suitability of applying NSAID in topical formulations applied to the skin. Oda desired minimal side effects as desired by applicants. One having ordinary skill in the art would have been manipulated the topical composition to achieve the desired delivery according to the condition to be treated. Therefore, it would have been obvious to one having ordinary skill in the art at the time of the invention to treat

migraine or tension headache by topical administration of NSAID as disclosed by US '861, and administer the NSAID topically to the skin in form of cream or patch as disclosed by US '874, motivated by the teaching of US '874 that topical administration of NSAID to the skin is extremely safe and causes little side effects, with reasonable expectation of successfully treating migraine or tension headache by administering to the skin a topical formulation comprising NSAID as the only active agent. In considering the disclosure of the reference, it is proper to take into account not only the specific teachings of the reference but also the inferences which one skilled in the art would reasonably be expected to draw therefrom. *In re Preda*, 401 F.2d 825, 826, 159 USPQ 342, 344 (CCPA 1968). The rational to modify or to combine the prior art does not have to be expressly stated in the prior art; the rational may be expressly or impliedly contained in the prior art or it may be reasoned from knowledge generally available to one of ordinary skill in the art. The reason or motivation to modify the reference may often suggest what the inventor has done, but for a different purpose or to solve different problem. It is not necessary that the prior art suggest the combination or modification to achieve the same advantage or result discovered by applicant. *In re Linter*, 458 F.2d 1013, 173 USPQ 560 (CCPA 1972).

See KSR Supreme Court of the United State Decision (Decided April 30, 2007, KSR INTERNATIONAL CO. v. TELEFLEX INC, et al. No. 04-1350) where it states That "However, the issue is not whether a person skilled in the art had the motivation to combine electronic control with an adjustable pedal assembly, but whether a person skilled in the art had the motivation to attach electronic control to the support bracket of

pedal assembly". In this present case, topical application of NSAID to the skin as the sole drug in the topical formulation as claimed would have been obvious to one skilled in the art at the time the invention was made because the prior art teaches the suitability of NSAID to be delivered topically to the skin and further teaches the ability of NSAID to treat migraine headache when it is the sole drug in the topical formulation used to treat headache.

It is well established that the claims are given the broadest interpretation during examination. A conclusion of obviousness under 35 U.S.C. 103 (a) does not require absolute predictability, only a reasonable expectation of success; and references are evaluated by what they suggest to one versed in the art, rather than by their specific disclosure. *In re Bozek*, 163 USPQ 545 (CCPA 1969).

In the light of the foregoing discussion, the Examiner's ultimate legal conclusion is that the subject matter defined by the claims would have been prima facie obvious within the meaning of 35 U.S.C. 103 (a).

5. The prior art made of record and not relied upon is considered pertinent to applicant's disclosure. The article "Migraine Headaches" teaches treating migraine by rubbing herbal medicinal formulation containing herbs known to treat migraine into the forehead and temples of the patients.

Conclusion

6. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

7. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Isis A. Ghali whose telephone number is (571) 272-0595. The examiner can normally be reached on Monday-Thursday, 7:00 to 5:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Woodward can be reached on (571) 272-8373. The fax phone number for the organization where this application or proceeding is assigned is (571) 273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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Art Unit 1615

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